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=> d his

    (FILE 'HOME' ENTERED AT 17:54:14 ON 18 OCT 2004)

    FILE 'REGISTRY' ENTERED AT 17:54:26 ON 18 OCT 2004
                E AMLODIPINE/CN
L1            1 S E3
                E ATORVASTATIN/CN
L2            1 S E3

    FILE 'CAPLUS' ENTERED AT 17:56:37 ON 18 OCT 2004
          1747 S L1 OR  AMLODIPINE OR PELMEC OR NORVASC
L4        1584 S L2 OR ATORVASTATIN OR LIPITOR
L5          19 S L3(L)L4
L6           0 S L5 NOT PY>=1999

    FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH' ENTERED AT 17:58:08 ON
    18 OCT 2004
L7           0 S L6
L8       13364 S  AMLODIPINE OR PELMEC OR NORVASC
L9       10180 S  ATORVASTATIN OR LIPITOR
L10        107 S L8(L)L9
L11          0 S L10 NOT PY>=1999

    FILE 'DRUGU, IMSRESEARCH' ENTERED AT 18:00:38 ON 18 OCT 2004
L12          3 S L11
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ANSWER 1 OF 3 DRUGU COPYRIGHT 2004 THE THOMSON CORP on STN
ESSION NUMBER: 1998-32025 DRUGU T E S
LE: Choosing the most appropriate treatment for stable angina. Safety considerations.
HOR: Asirvatham S; Sebastian C; Thadani U
PORATE SOURCE: Univ.Oklahoma
CATION: Oklahoma City, Okla., USA
RCE: Drug Safety (19, No. 1, 25-44, 1998) 5 Tab. 142 Ref.
CODEN: DRSAE ISSN: 0114-5916
IL. OF DOC.: Division of Cardiology, University of Oklahoma Health Sciences Center, 920 SL Young, 5SP-300, Oklahoma City, OK 73190, U.S.A. (U.T.).
NGUAGE: English
CUMENT TYPE: Journal
LD AVAIL.: AB; LA; CT
LE SEGMENT: Literature
1998-32025 DRUGU T E S
The treatment of stable angina is reviewed with reference to safety considerations. The pathophysiology, natural history and prognosis of stable angina are discussed. Drug therapy for plaque stabilization, prevention of MI and mortality reduction is discussed with reference to aspirin, ticlopidine, lipid lowering therapy, estrogen supplementation, ACE-inhibitors and antioxidants. Symptomatic treatment with nitrates, beta-blockers and Ca2+ antagonists is considered. Guidelines for choosing appropriate drug or combination therapy for stable angina are given.
EX Aspirin reduces mortality and morbidity in patients with acute coronary syndromes. Its main adverse effects are GI. It interacts with warfarin, corticosteroids, NSAID, alcohol and uricosuric drugs. Ticlopidine is used as an alternative to aspirin in patients with stable angina pectoris. Drugs used to lower serum lipids include colestyramine, colestipol, nicotinic acid, fluvastatin, lovastatin, simvastatin, gemfibrozil and probucol. Colestipol and colestyramine interact with digoxin, warfarin and phytomenadione. Mibefradil can interact with lovastatin or simvastatin. Estrogen supplementation in postmenopausal women can reduce the risk of coronary artery disease, but can increase the risk of breast cancer, endometrial hyperplasia and thrombosis. ACE-inhibitors (enalapril, fosinopril, ramipril, captopril, benazepril and quinapril) may also be useful for the treatment of stable angina. Adverse effects include cough, hypotension, renal effects, angioedema and hyperkalemia. ACE-inhibitors interact with furosemide, hydralazine, indometacin and aspirin. Antioxidants (tocopherol, beta-carotene and retinol) may protect against coronary artery disease. Effort angina is treated with isosorbide dinitrate, isosorbide mononitrate and nitroglycerol. Beta-blockers (propranolol, metoprolol) can be used to reduce myocardial ischemia. They interact with verapamil, lidocaine and phenytoin. Ca2+ antagonists (verapamil, nifedipine, **amlodipine**, felodipine, diltiazem and mibefradil) are often used to treat angina pectoris. They may interact with quinidine, digoxin, rifampicin, carbamazepine, ciclosporin, **atorvastatin**, terfenadine, astemizole, cisapride and cerivastatin. (E83)

2 ANSWER 2 OF 3 DRUGU COPYRIGHT 2004 THE THOMSON CORP on STN
CESSION NUMBER: 1998-29103 DRUGU P T S
TLE: Mibefradil, a pharmacologically distinct calcium antagonist.
THOR: Ernst M E; Kelly M W
RPORATE SOURCE: Univ.Iowa
CATION: Iowa City, Iowa, USA
URCE: Pharmacotherapy (18, No. 3, 463-85, 1998) 4 Fig. 5 Tab. 100 Ref.
CODEN: PHPYDQ ISSN: 0277-0008
AIL. OF DOC.: College of Pharmacy, The University of Iowa, S411 Pharmacy Building, Iowa City, IA 52242, U.S.A.
NGUAGE: English
CUMENT TYPE: Journal
ELD AVAIL.: AB; LA; CT
LE SEGMENT: Literature

1998-29103 DRUGU P T S
The characteristics of mibefradil (MB, (1S,2S)-2-)2-((3-(2-benzimidazoyl) propyl)methylamino)ethyl)- 6-fluoro-1,2,3,4-tetrahydro- 1-isopropyl-2-naphthylmethoxyacetate HCl2) are reviewed, with reference to its chemistry, pharmacology, pharmacokinetics, pharmacodynamics, efficacy in animal models and patients with hypertension, chronic stable angina pectoris and heart failure, adverse events and drug interactions. Other Ca antagonists mentioned include diltiazem, verapamil, **amlodipine**, felodipine and nifedipine. Agents investigated for interactions with MB include terfenadine, astemizole, cisapride, lovastatin, simvastatin, **atorvastatin**, cerivastatin, pravastatin, digoxin, fluvastatin, quinidine, imipramine, desipramine, enalapril, atenolol, cimetidine, theophylline, warfarin and phenytoin.

EX MB is the prototype of a new class of Ca antagonists that selectively block T-type voltage-gated plasma membrane calcium channels in vascular smooth muscle. MB is structurally and pharmacologically different from traditional Ca antagonists such as diltiazem and verapamil. MB dos not have negative inotropic effects at therapeutic concentrations and is not associated with reflex activation of neurohormonal and sympathetic systems. In patients with hypertension, MB at 50 and 100 mg/day reduces trough sitting diastolic and systolic B.P. Doses of over 100 mg/day do not increase efficacy, but were associated with a greater frequency of side-effects. MB has antiischemic properties resulting from dilation of coronary and peripheral vascular smooth muscle, and from a slight reduction in HR. In clinical studies of chronic stable angina pectoris, MB leads to dose-dependent increases in exercise duration and time to onset of angina. MB reduces the number and duration of ischemic events, the number of anginal episodes and nitroglycerol consumption. MB has a favorable pharmacokinetic profile, with a high trough:peak ratio (over 80%), good oral bioavailability and a long-elimination half-life. Dizziness, headache, leg edema and lightheadedness are frequently reported with MB. The most frequent EEG changes associated with MB are 1st-degree A.V. block and sinus bradycardia. In-vitro, MB inhibited cytochrome P450 1A2, 2D6 and 3A4 and should thus not be given with terfenadine, astemizole, cisapride, lovastatin, simvastatin, **atorvastatin** and cerivastatin. The dose of MB should be reduced when it is given with imipramine or desipramine. (E61/MB)

2 ANSWER 3 OF 3 DRUGU COPYRIGHT 2004 THE THOMSON CORP on STN
CESSION NUMBER: 1998-25850 DRUGU T P E S
TLE: Drug administration in patients with diabetes mellitus. Safety considerations.
THOR: Gilbert R E; Cooper M E; Krum H
RPORATE SOURCE: Univ.Melbourne; Univ.Monash
CATION: Melbourne, Austr.
URCE: Drug Safety (18, No. 6, 441-55, 1998) 2 Tab. 96 Ref.
CODEN: DRSAE ISSN: 0114-5916
AIL. OF DOC.: Endocrinology Unit, Austin and Repatriation Medical Centre (Austin Campus), Studley Road, Heidelberg, Victoria 3084, Australia.
NGUAGE: English
CUMENT TYPE: Journal
ELD AVAIL.: AB; LA; CT
LE SEGMENT: Literature
1998-25850 DRUGU T P E S
The drugs used in patients with diabetes mellitus are reviewed, with emphasis on safety considerations. Areas covered in the review include the effect of diabetes mellitus on drug handling, drugs used to control hyperglycemia in these patients, including metformin, the sulfonylureas, newer agents such as troglitazone and acarbose and insulin and drugs used to treat diseases associated with diabetes mellitus included antihypertensives and lipid-lowering agents.

EX Drug dose adjustment is rarely required where diabetes mellitus is well controlled. In the context of poor metabolic control or in the presence of complications such as nephropathy, significant alterations in drug handling may occur. Rarely, metformin use may be complicated by lactic acidosis. Long-term metformin may impair the absorption of cyanocobalamin and folate. The sulfonylureas chlorpropamide and

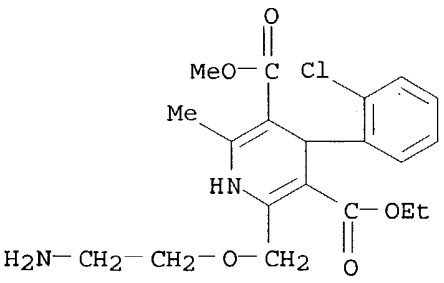
glibenclamide have longer durations than glipizide, glicazide or tolbutamide. Other sulfonylureas include tolazamide and acetohexamide. Long-acting sulfonylureas are best avoided in patients at high risk of hypoglycemia. The latter may be potentiated by drug interactions with phenytoin, rifampicin, warfarin, phenylbutazone and salicylates. Sulfonylureas may also interact with antacids, histamine H2 antagonists, omeprazole, beta-blockers, steroids, ACE inhibitors, perhexiline, chloramphenicol, ciprofloxacin, clofibrate, diuretics, dicoumarol, fluconazole, ketoconazole, fluoxetine, phenelzine, isocarboxazid, tranylcypromine and oxyphenbutazone. Troglitazone may be associated with abnormalities in liver function in about 2% of patients. The adverse effects of acarbose tend to improve with continued therapy. Drugs used to treat diseases associated with diabetes mellitus include ACE inhibitors such as enalapril, Ca antagonists such as nisoldipine, fosinopril and **amlodipine**, beta-blockers such as carvedilol, diuretics, HMG CoA reductase inhibitors such as lovastatin, pravastatin, simvastatin, fluvastatin and **atorvastatin**, and the fibrate derivatives clofibrate, gemfibrozil, bezafibrate or fenofibrate. (E61/MB)

L13 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2004 ACS on STN
RN 111470-99-6 REGISTRY

**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

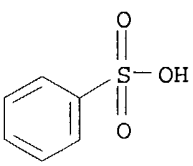
CN 3,5-Pyridinedicarboxylic acid, 2-[(2-aminoethoxy)methyl]-4-(2-chlorophenyl)-1,4-dihydro-6-methyl-, 3-ethyl 5-methyl ester, monobenzenesulfonate (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Benzenesulfonic acid, compd. with 3-ethyl 5-methyl 2-[(2-aminoethoxy)methyl]-4-(2-chlorophenyl)-1,4-dihydro-6-methyl-3,5-pyridinedicarboxylate (1:1)
OTHER NAMES:
CN (±)-3-Ethyl 5-methyl 2-[(2-aminoethoxy)methyl]-4-(2-chlorophenyl)-1,4-dihydro-6-methyl-3,5-pyridinedicarboxylate monobenzenesulfonate
CN Amcard
CN Amdepin
CN Amdipin
CN Amlodin
CN Amlodipine benzenesulfonate
CN Amlodipine benzenesulfonate salt
CN Amlodipine besylate
CN Amlopin
CN Amlor
CN Amlosyn
CN Antacal
CN Calchek
CN Istin
CN Lowrac
CN Monopina
CN Norvas
CN **Norvasc**
CN Norvask
CN Tensivask
CN UK 48340-26

CM 1




**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

CM 2



**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**